REMARKS

Status of Claims and Claim Amendments

Claim 4 is amended to correct an inadvertent typographical error; that is, it is amended to depend from claim 3 rather than from itself. Claims 4, 7, 14 and 19 are amended to clarify the invention being claimed, as more fully discussed below. Claim 11 is amended to present it in independent form, as discussed further below. The amendments to claims 4, 7, 11, 14 and 19 are not made for substantive reasons related to patentability. They do not narrow or surrender any of the subject matter of the claims as originally filed, but are made merely for purposes of clarification.

Claims 17, 22 and 23 are amended to remove reference to R^3 being heteroarylalkoxy and claims 20 and 21 are canceled, which amendments are made without prejudice.

All of the claim amendments herein have been made without prejudice and without acquiescing to any of the Examiner's objections or rejections. Applicants reserve the right to file any of the cancelled subject matter in a continuing patent application.

Applicants submit that no new matter has been added to the claims as a result of these amendments and that the amended claims submitted herewith are fully supported by the application as originally filed. Entry of the claim amendments is respectfully requested.

Claim Objection

Claim 11 has been objected to as being dependent on a rejected base claim.

Response: While Applicants do not agree that the base claims from which claim 11 depends are improper, in order to expedite prosecution of this application claim 11 has been re-written herein in independent form.

In view of this, it is believed that claim 11 is in condition for allowance.

Rejections of Claims 4, 7, 14, 19 and 21 under 35 U.S.C. §112, 2¶

1. Claim 4 stands rejected as being indefinite because it depends from itself.

Response: This inadvertent typographical error has been corrected by amendment herein, so that claim 4 now depends from claim 3.

2. Claims 4, 7, 14, 19 and 21 each recite "compound" in the preamble but, according to the Office Action, what is covered is species in a particular solvent.

Response: Applicants respectfully disagree with the interpretation of the claims as stated in the Office Action as grounds for this rejection. These claims have been amended to delete reference to a solvent, as that is not, in fact, what Applicants are claiming. They are claiming a compound or its pharmaceutically acceptable salt, which salt may be a trifluoroacetic acid salt, an acetic acid salt or a trifluoro-ethanediol salt. This is discussed in more detail in the discussion below concerning the rejection under 35 U.S.C. §112, 1¶, to which the Examiner's attention is directed.

In view of the above discussions, it is requested that the rejections under the second paragraph of §112 be withdrawn.

Rejection of Claims 1-10 and 12-23 under 35 U.S.C. §112, 1¶

Claims 1-10 and 12-23 stand rejected as not being enabling. More specifically, it is stated that the claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention; that is, that several of the compounds claimed are not obtained in the free form but rather are isolated in a solvent mixture and that the solvents employed are not suitable solvents for therapeutic purposes. The Office Action further states that the specification is silent as to how these compounds can be further purified or if they are only stable in the solution.

Response: Applicants respectfully traverse this rejection. The Office Action has not made out a *prima facie* case of nonenablement. The teachings in the specification must be looked at in view of the state of the art and the knowledge of one of ordinary skill in the art to determine whether the specification is enabling. First, Applicants disagree with the characterization of the claims made in the Office Action; that is, that the claims are directed to compositions of a compound in a solvent. This is incorrect. The claims are in fact directed to compounds and their pharmaceutically acceptable salts. This is clearly stated in the claims and supported in the specification as filed. "Pharmaceutically acceptable salts" are defined in the specification at page 15, lines 1-23, and specifically include, e.g., acetic acid and trifluoroacetic acid (TFA) as examples of pharmaceutically acceptable salts. Additionally, at (for example) page 51, lines 11-19, of the specification, in describing the synthesis of a particular compound the following language is found: "The solvent was evaporated and purified by preparative HPLC to afford 2-[1S-(4-(ethoxycarbonyl)piperazin-

1-yl)carbonyl-3-carboxypropyl]aminocarbonyl-7-methyl-6-chloro-4-(1-phenyl-1-carboxy)methoxyquinoline *in trifluoroacetic acid, as a white solid* (116 mg, 66%) *as a TFA salt* . . . ." [lines 14-17, emphasis added]. Thus, the solvent was removed from the compound, giving a white solid salt. It is clear from the descriptions of the syntheses in the specification that a compound (or a salt thereof) and not a solvent composition is what the inventors have made and what they regard as their invention.

In addition, it is well known to those skilled in the art that when certain solvents are used in the purification of chemical compounds, they often remain in the purified compound in a minute amount as a salt. Thus, for example, trifluoroacetic acid (TFA) is used as a solvent in reversed-phase HPLC separation and in LCMS, and it is known that for compounds with a basic center, a small amount of TFA remains in the sample via formation of the corresponding TFA salt.

Those of skill in the art would understand from the descriptions in the specification, as well as from the common knowledge in the art, how to make and use the claimed invention. Further, the claims as originally filed include the pharmaceutically acceptable salts of the compounds (see, e.g., the last line of independent claim 1). In view of this, the further inclusion of "in acetic acid" or "in trifluoroacetic acid", for example, has been deleted from the present claims by amendment herein as being redundant.

The statement in the Office Action that the claimed solvents [although Applicants wish to clarify that the claims are not directed to compounds in a solvent] are not suitable for therapeutic purposes is incorrect. Peptides, for example, are generally commercially available as TFA salts. As just two examples found by a quick Google search on the internet: 1) Chemicon International sells recombinant human beta amyloid 1-42, R5G, ***TFA*** (product #AG926) [emphasis added] (www.chemicon.com/Product/ProductDataSheet.asp?ProductItem=AG926); Chemicon's datasheet states that "The TFA salt is what has been the industry standard"; and 2) Axxora sells hGRF(1-44), **TFA-salt** [emphasis added] (www.axxora.com/growth_factors_cytokines_chemokines-PBL-11972/opfa.1.1.PBL-11972). Obviously, TFA salts of peptides and other therapeutics are commonly available and commonly used. In addition, acetic acid is approved by the FDA as an additive. Thus, salts such as acetic acid salts and TFA salts are indeed suitable.

With respect to the statement that the specification is silent as to how the compounds can be further purified, firstly it is not always necessary to further purify the

pharmaceutically acceptable salts of the invention (see discussion above). For example, the compounds of the invention may be used as standard or reference compounds (see, e.g., p. 17, line 32 - p. 18, line 4). If purification were desired, it was commonly known in the art at the time the invention was made that salts such as acetic acid or TFA salts, e.g., can be converted to a hydrochloride or biologically equivalent salt by processes generally known to those of skill in the art. See, e.g., J. Cornish et al., *Am J Physiol Endocrinol Metab* 277: E779-E783 (1999), which discusses TFA salts of peptides and includes discussion of how to convert them to the HCl salt. When something is generally known in the art, as here, it is not necessary for the specification to disclose it in order for the specification to be enabling.

As discussed above, the specification is enabling under the first paragraph of §112, and it is respectfully requested that this rejection be withdrawn.

Rejection under the Doctrine of Obviousness-Type Double Patenting

Claims 17, 20, 22 and 23 stand rejected as being unpatentable over claims 1-8, 59 and 60 of U.S. Pat. No. 6,861,424.

Response: In order to expedite prosecution of the present application, claims 17, 22 and 23 have been amended to remove "heteroarylalkoxy" as a value for R^3. Claims 20 and 21 have been deleted, as they are specifically directed to R^3 = heteroarylalkoxy. These amendments are made without prejudice to claiming this cancelled subject matter in a continuing application.

In view of these amendments, it is believed that is rejection is now moot and it is requested that the rejection be withdrawn.

CONCLUSION

The Office Action dated June 27, 2005 has been carefully considered. It is believed that the amendments submitted herewith and the above comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

Respectfully submitted,

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